

AMENDMENTS TO THE SPECIFICATION

Please delete the sequence listing from the present application and replace with the sequence listing submitted on paper copy attached herewith.

In the specification at page 1, after the title and before line 3, please insert the following new paragraph and headings:

RELATED APPLICATIONS

This application is a national stage application (under 35 U.S.C. 371) of PCT/EP2003/009106 filed August 18, 2003 which claims benefit to German application 102 38 980.2 filed August 20, 2002, German application 102 38 978.0, filed August 20, 2002, German application 102 38 979.9 filed August 20, 2002, German application 102 53 112.9 filed November 13, 2002, and German application 102 58 971.2 filed December 16, 2002.

BACKGROUND OF THE INVENTION

In the specification at page 2, line 21, please insert the following headings and description of the figures:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts the chromatographic analysis of a sample obtained from an *E. coli* strain transformed with pNOSTF-G and pMCL-CrtYIBZ/idi/gps. This strain is shown to be able to synthesize various ketocarotenoids, owing to heterologous complementation. Astaxanthin (peak 1), adonirubin (peak 2) and canthaxanthin (peak 3) are eluted with increasing retention time.

Figure 2 depicts the chromatographic analysis of a sample obtained from an *E. coli* strain transformed with the expression vector as described in Example 3.1 and pMCL-CrtYIBZ/idi/gps. With use of a *Haematococcus pluvialis* ketolase, as described, for example, in EP 725137, astaxanthin (peak 1), adonixanthin (peak 2) and unreacted zeaxanthin (peak 3) are eluted with increasing retention time.

Figure 3 shows the construct map of the expression vector pS3FNR:NOST (MSP101).

Figure 4 shows the construct map of the expression vector pS5FNR:NOST (MSP102).

Figure 5 shows the construct map of the expression vector pS3AP3:NOST (MSP103).

Figure 6 shows the construct map of the expression vector pS5AP3:NOST (MSP104).

Figure 7 shows the construct map of the expression vector pS3FNR:NP196 (MSP105).

Figure 8 shows the construct map of the expression vector pS5FNR:NP196 (MSP106).

Figure 9 shows the construct map of the expression vector pS3EPS:NP196 (MSP107).

Figure 10 shows the construct map of the expression vector pS5EPS:NP196 (MSP108).

Figure 11 shows the construct map of the expression vector pS3FNR:NP195 (MSP109).

Figure 12 shows the construct map of the expression vector pS5FNR:NP195 (MSP110).

Figure 13 shows the construct map of the expression vector p35EPS:NP195 (MSP111).

Figure 14 shows the construct map of the expression vector pS5EPS:NP195 (MSP112).

Figure 15 shows the construct map of the expression vector pS3FNR:NODK (MSP113).

Figure 16 shows the construct map of the expression vector pS5FNR:NODK (MSP114).

Figure 17 shows the construct map of the expression vector pS3EPS:NODK (MSP115).

Figure 18 shows the construct map of the expression vector pS5EPS:NODK (MSP116).

DETAILED DESCRIPTION OF THE INVENTION

In the specification at page 26, line 17, please replace the paragraphs starting with “pTP09” with the following amended paragraphs:

pTP09

KpnI_GGTACCATGGCGTCTTCTTCTTCTCTCACTCTCTCTCAAGCTATCCTCTCTCGTT
CTGTCCCTCGCCATGGCTCTGCCTCTTCTTCTCAACTTTCCCCTTCTTCTCTCACTTTT
TCCGGCCTTAAATCCAATCCCAATATCACCACTCCCGCCGCCGTACTCCTTCCTCCG
CCGCCGCCGCCGCCGTCTGTAAGGTCACCGGCGATTCTGTCCTCAGCTGCAACCGAA
ACCATAGAGAAAAGTGAAGTGCAGGATCC_BamHI (SEQ ID NO: 75)

pTP10

KpnI_GGTACCATGGCGTCTTCTTCTTCTCACTCTCTCTCAAGCTATCCTCTCTCGTT
CTGTCCCTCGCCATGGCTCTGCCTCTTCTTCTCAACTTTCCCCTTCTTCTCACTTTT
TCCGGCCTTAAATCCAATCCCAATATCACACCTCCCGCCGCCGTACTCCTTCCTCCG
CCGCCGCCGCCGCCGTCGTAAGGTCACCGGCGATTCTGTGCCTCAGCTGCAACCGAA
ACCATAGAGAAAAGTGAAGTGGCTGGATCC_BamHI (SEQ ID NO: 76)

pTP11

KpnI_GGTACCATGGCGTCTTCTTCTTCTCACTCTCTCTCAAGCTATCCTCTCTCGTT
CTGTCCCTCGCCATGGCTCTGCCTCTTCTTCTCAACTTTCCCCTTCTTCTCACTTTT
TCCGGCCTTAAATCCAATCCCAATATCACACCTCCCGCCGCCGTACTCCTTCCTCCG
CCGCCGCCGCCGCCGTCGTAAGGTCACCGGCGATTCTGTGCCTCAGCTGCAACCGAA
ACCATAGAGAAAAGTGAAGTGGGATCC_BamHI (SEQ ID NO: 77)

In the specification at page 44, line 6, please replace the paragraph starting with “The clone pCB-gps” with the following amended paragraph:

The clone pCB-gps was therefore used for cloning the *gps* gene into the pMCL-CrtYIBZ/idi vector. Cloning was carried out by isolating the KpnI/XhoI fragment from pCB-gps and ligating it into the pMCL-CrtYIBZ/idi vector cut with KpnI and XhoI. The cloned KpnI/XhoI fragment (SEQ ID NO. 34) carries the Prn16 promoter together with a minimum 5' UTR sequence of *rbcL*, the first 6 *rbcL* codons which extend the GGPP synthase N-terminally, and, 3' from the *gps* gene, the *psbA* sequence. Thus, the N terminus of GGPP synthase has, instead of the natural amino acid sequence with Met-Leu-Lys-Glu (amino acids 1 to 4 of AF120272, SEQ ID NO: 78), the altered amino acid sequence Met-Thr-Pro-Gln-Thr-Ala-Met-Val-Lys-Glu (SEQ ID NO: 79). This leads to recombinant GGPP synthase, starting with Lys at position 3 (in AF120272), being identical and having no other changes in the amino acid sequence. The *rbcL* and *psbA* sequences were used according to a reference by Eibl et al. (Plant J. 19. (1999), 1-13). The resulting clone is referred to as pMCL-CrtYIBZ/idi/gps.

In the specification at page 46, line 18, please replace the paragraphs starting with "For cDNA synthesis" with the following amended paragraphs:

For cDNA synthesis, 2.5 µg of total RNA were denatured at 60°C for 10 min, cooled on ice for 2 min and transcribed into cDNA by means of a cDNA kit (Ready-to-go-you-prime-beads, Pharmacia Biotech), according to the manufacturer's information using an antisense-specific primer, PR1 (gcaagctcga cagctacaaa cc, SEQ ID NO: 80).

The nucleic acid encoding a ketolase from *Haematococcus pluvialis* (strain 192.80) was amplified by means of polymerase chain reaction (PCR) from *Haematococcus pluvialis*, using a sense-specific primer, PR2 (gaagcatgca gctagcagcg acag, SEQ ID NO: 81), and an antisense-specific primer, PR1.

In the specification at page 47, line 10, please replace the paragraph starting with "PCR amplification with" with the following amended paragraph:

PCR amplification with PR1 and PR2 resulted in a 1155 bp fragment which encodes a protein consisting of the entire primary sequence:

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gaagcatgca gctagcagcg acagtaatgt tggagcagct taccggaagc gctgaggcac      60
tcaaggagaa ggagaaggag gttgcaggca gctctgacgt gttgcgtaca tgggcgaccc      120
agtactcgct tccgtcagag gagtccagcg cggcccgcgc gggactgaag aatgcctaca      180
agccaccacc ttccgacaca aaggccatca caatggcgct agctgtcatc ggctcctggg      240
ccgcagtgtt cctccacgcc atttttcaaa tcaagcttcc gacctccttg gaccagctgc      300
actggctgcc cgtgtcagat gccacagctc agctgggttag cggcagcagc agcctgctgc      360
acatcgctcg agtattcttt gtcctggagt tcctgtacac aggccttttt atcaccacgc      420
atgatgctat gcatggcacc atcgccatga gaaacaggca gcttaatgac ttcttgggca      480
gagtatgcat ctccctgtac gcctgggttg attacaacat gctgcaccgc aagcattggg      540
agcaccacaa ccacactggc gaggtgggca aggaccctga cttccacagg ggaaaccctg      600
gcattgtgcc ctggtttgcc agcttcatgt ccagctacat gtcgatgtgg cagtttgcgc      660
gcctcgcatg gtggacgggtg gtcatgcagc tgctgggtgc gccaatggcg aacctgctgg      720

tggttcatggc ggccgcgccc atcctgtccg cttccgcgtt gttctacttt ggcacgtaca      780
tgccccacaa gcctgagcct ggccgcgctt caggctcttc accagcgcgc atgaactggg      840
ggaagtgcgc cactagccag gcgtccgacc tggtcagctt tctgacctgc taccacttcg      900
acctgcactg ggagcaccac cgctggccct ttgcccctg gtgggagctg cccaactgcc      960
gccgcctgtc tggccgaggt ctggttcctg ctagctgga cactactgcag tgggccctgc     1020
tgccagctgg gcatgcaggt tgtggcagga ctgggtgagg tgaaaagctg caggcgctgc     1080
tgccggacac gctgcatggg ctaccctgtg tagctgccgc cactagggga ggggggttgt     1140
agctgtcgag cttgc
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(SEQ ID NO: 82).